

COMPARATIVE EVALUATION OF THE EFFICACY, SAFETY AND QUALITY OF LIFE WITH THE TREATMENT OF ROSUVASTATIN AND ATORVASTATIN IN DYSLIPIDEMIA PATIENTS

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ABSTRACT

Background and Aim : Lipid lowering drugs provide benefit in patients across the entire spectrum of cholesterol levels; primarily by reducing levels of low-density lipoprotein cholesterol. This study is to assess the percentage reduction in lipid levels achieved in Rosuvastatin and Atorvastatin in dyslipidemic patients and also to define patient groups who are at high risk for dyslipidemia and analyse the percentage of adverse effect in Rosuvastatin and Atorvastatin.

Materials and Methods: This study enrolled 60 patients and divided into four groups of 15 patients in each group. Group-1 patients received Rosuvastatin 10 mg tablet once in a day, Group-2 received

Atorvastatin 20 mg tablet once in a day, Group-3 patients received Rosuvastatin 20 mg tablet once in a day, and Group-4 received Atorvastatin 40 mg tablet once in a day for a period of 20 weeks. **Results :** Statistical analysis using student unpaired t-test shows that Rosuvastatin 10mg is better than Atorvastatin 20mg and also shows that Rosuvastatin 20mg is better than Atorvastatin 40mg in the reduction of total cholesterol, Low density lipoprotein, Triglycerides and in increasing of HDL and found to be statistically significant. The comparison of Diastolic and systolic Blood Pressure in rosuvastatin and atorvastatin patients did not show any significant difference. The Side effects differed between the rosuvastatin and atorvastatin groups; the incidence of Side effects in rosuvastatin and atorvastatin patients is not statistically significant. **Conclusion :** Patients treated with rosuvastatin had significantly greater reductions in LDL cholesterol, total cholesterol, triglycerides levels compared with

those receiving atorvastatin. Patients receiving rosuvastatin were more likely to attain lipid goals compared with patients treated with atorvastatin.

KEY WORDS : Dyslipidemia, Rosuvastatin, Atorvastatin.

INTRODUCTION

Dyslipidemia refers to an abnormality within the lipid profile, encompassing a variety of disorders relating to elevations in total cholesterol, LDL, or TG, or conversely, lower levels of HDL. The dyslipidemia may present as a single disorder affecting only one lipoprotein parameter, or may represent a combination of lipoprotein abnormalities, such as elevated TG and low HDL. A dyslipidemia may be the result of over-production or lack of clearance of the lipoprotein particles, or related to other defects in the apolipoproteins or enzyme deficiencies. The pathways and means of lipid metabolism in the human body reflect complex processes, and genetics, certain medical conditions, medications, and/or environmental factors may influence lipoprotein metabolism in some capacity, resulting in a dyslipidemia condition. In the clinical setting, a primary dyslipidemia typically refers to a genetic defect in the lipid metabolism as a cause of the problem [1]. A secondary dyslipidemia may be attributed to another cause. For example, environmental factors (such as a diet rich in saturated fat or a sedentary lifestyle), diseases (such as diabetes, hypothyroidism, obstructive liver disease), and medications (such as thiazide diuretics, progestins, or anabolic steroids) may result in a secondary dyslipidemia [2,3].

The current NCEP guidelines for management of patients are of two types. One is a population-based approach to reduce CHD risk, which includes recommendations to increase exercise (to expend ~2000 calories/week) and to lower blood cholesterol by dietary recommendations: reduce total calories from fat to less than 30% and from saturated and trans fats to less than 10%; consume less than 300 mg of cholesterol per day; eat a variety of oily fish twice a week [4] and oils/foods rich in linolenic acid (canola, flaxseed, and soybean oils, flaxseed, and walnuts); and maintain desirable body weight. The second is the patient-based approach that focuses on lowering LDL-C levels as the primary goal of therapy [5]. The guidelines for the management of adults 20 years and older recommend a complete fasting lipoprotein profile (total cholesterol, LDL-C, HDL-C, and triglycerides).

Diabetic dyslipidemia is usually characterized by high triglycerides, low HDL-C, and moderate elevations of total cholesterol and LDL-C. In fact, diabetics without diagnosed

CHD have the same level of risk as no diabetics with established CHD [6]. Thus, the dyslipidemia treatment guidelines for diabetic patients are the same as for patients with CHD, irrespective of whether the diabetic patient has had a CHD event. The first line of treatment for diabetic dyslipidemia usually should be a statin [7].

Recognition that dyslipidemia is a risk factor has led to the development of drugs that reduce cholesterol levels. These drugs provide benefit in patients across the entire spectrum of cholesterol levels, primarily by reducing levels of low-density lipoprotein cholesterol (LDL-C). In well-controlled clinical trials, fatal and nonfatal CHD events and strokes were reduced by as much as 30% to 40% [8-14].

Atorvastatin affects diabetic kidney disease and whether the effect of atorvastatin on cardiovascular disease (CVD) varies by kidney status in patients with diabetes. A modest beneficial effect of atorvastatin on eGFR, particularly in those with albuminuria, was observed [15]. Rosuvastatin significantly decreased LDL-C and total cholesterol compared to atorvastatin (-45.5% vs. -37.9% in LDL-C, $p < 0.0001$). Rosuvastatin decreased sharp more significantly [16]. Any comparison of statins requires scrutiny of the relation between therapeutic effect and risk of side effects. This report sought to determine whether the additional LDL cholesterol lowering with rosuvastatin over atorvastatin could be obtained without increased risk of short-term adverse events [17].

METHODOLOGY

This study was conducted in **meenakshi mission hospital and research centre (mmhrc)** in Madurai.

Study design: Randomized, Prospective and Comparative Study.

Sample size: 60 patients

A total of 60 patients were included in the study in four groups of 15 patients in each group. Group-1 patients received rosuvastatin 10 mg tablet once in a day, Group-2 received atorvastatin 20 mg tablet once in a day, Group-3 patients received rosuvastatin 20 mg tablet once in a day, and Group-4 received atorvastatin 40 mg tablet once in a day for a period of 20 weeks. Pre index laboratory test values for the 5 month period before statin initiation were collected. Post index laboratory test values were captured after 9 weeks. At each follow visit, patient were assessed for lipid profile, adverse effect was asked. The patients were reviewed, and the lipid and safety profiles were repeated. Patients measure the lipid level (LDL cholesterol, HDL cholesterol, Total cholesterol and triglycerides). Patients were asked to

report their assessment of side effects during the study. The Pre index or Post index period was used to estimate the percentage change in lipid values for each laboratory value and to determine the efficacy, safety and quality of life in dyslipidemia patient.

Inclusion Criteria

1. Patients aged ≥ 18 years with hypercholesterolemia and a history of CHD,
2. Clinical evidence of atherosclerosis or a CHD-risk equivalent (other clinical form of atherosclerotic disease [peripheral arterial disease, abdominal aortic aneurysm or symptomatic carotid artery disease (transient ischemic attacks, stroke of carotid origin, or $> 50\%$ obstruction of a carotid artery)])
3. Baseline levels of LDL-C $> 100\text{mg/dl}$
4. HDL-C $< 40\text{mg/dl}$
5. Total cholesterol $> 200\text{mg/dl}$
6. Triglycerides $> 200\text{mg/dl}$ and $< 500\text{mg/dl}$
7. Diabetes mellitus or ≥ 2 risk factors that confer a 10-year CHD-risk score $> 20\%$ were eligible for randomization to the study.

Exclusion Criteria

1. A history of hypersensitivity to statins
2. Pregnancy / lactation
3. Active liver diseases / hepatic dysfunction
4. Patients having history of severe myalgia or myositis.
5. Serious or unstable medical or psychological condition that could compromise the patient's safety or successful trial participation.

Statistical Tool

The information collected regarding all the selected cases were recorded in a Master Chart. Data analysis was done with the help of computer using Graph Pad InStat DTCG (GPI v3.0). Using this software frequencies, percentages, means, standard deviations, Student unpaired t-test and 'p' values were calculated. Student unpaired t-test was used to test the significance of difference between quantitative variables and Yate's test for qualitative variables. A 'p' value less than 0.05 is taken to denote significant relationship.

RESULTS

Clinical Characteristics

In this study totally 100 patients were examined. 80 of them had CAD. Due to side effects and other reasons 20 patients discontinued from treatment. Only 60 patients of them had regular treatment. The baseline clinical characteristics of patients with rosuvastatin and atorvastatin are summarized in the table. Out of the 60 patients in the study Diabetes was present in 20(20%) and Hypertension in 32(32%) at baseline. These patients were significantly older, had a higher systolic BP and a higher incidence of Hypertension.

Age Distribution

Although the age differed between the rosuvastatin and atorvastatin group, the incidence of dyslipidemia in patients older than 50 years were higher when compared with younger patients. Statistical analysis using student unpaired t- test shows that the p-value is 0.3396 and 0.0773 since the p value is greater than 0.05 the incidence of Dyslipidemia in elderly patients is not statistically significant.

Comparative Efficacy

It shows that Rosuvastatin 10mg is better than Atorvastatin 20mg in the reduction of total cholesterol and also shows that Rosuvastatin 20mg is better than Atorvastatin 40mg in the reduction of total cholesterol. Statistical analysis using student unpaired t- test shows that the p value is less than 0.05; the total cholesterol in patient between rosuvastatin and atorvastatin are found to be statistically significant. The comparison of total cholesterol in Rosuvastatin and Atorvastatin patients were found to be statistically significant. (Table 1)

Table.1 Changes in Total Cholesterol

Total cholesterol values at	Rosuvastatin 10mg	Atorvastatin 20mg	P value	Rosuvastatin 20mg	Atorvastatin 40mg	P value
First visit	210.3±16	216.9±18.1	0.1495	243.4±47.1	234.9±34.1	0.6184
Second visit	189.1±3.6	206.7±2.6	0.0354	217.7±4.2	206.3±6.5	0.0231
Third visit	165.4±27.1	182.5±7.9	0.0318	172.4±4.7	180.6±4.1	0.0432
Changes during						
Second visit	21.1±18.4	10.1±7.5	0.0195	35.7±4.2	28.5±3.3	0.0177
Third visit	46.6±22.7	34.4±7.3	0.0472	68.9±6.2	58.1±7.9	0.0256
% of changes during						
Second visit	10.1±4.0	4.3±3.2	0.00214	15.0±2.9	11.4±2.5	0.0457
Third visit	22.1±2.7	15.7±3.9	0.047	25.4 ±4.2	22.7±3.7	0.0277

It shows that Rosuvastatin 10mg is better than Atorvastatin 20mg increase of HDL and also shows that Rosuvastatin 20mg is better than Atorvastatin 40mg increase of HDL. Statistical analysis using student unpaired t-test shows that the p value is less than 0.05; the total cholesterol in patient between rosuvastatin and atorvastatin are found to be statistically significant. The comparison of HDL in rosuvastatin and atorvastatin patients was found to be statistically significant. (Table 2)

Table.2 Changes in HDL

HDL values at	Rosuvastatin 10mg	Atorvastatin 20mg	P value	Rosuvastatin 20mg	Atorvastatin 40mg	P value
First visit	40.7±4.7	40.7±4.8	0.9523	41.9±6.2	41.5±4.9	0.6466
Second visit	43.5±3.7	42±6.8	0.1172	46.5±2.4	43.5±3.5	0.0489
Third visit	46.9±4.2	42.3±3.6	0.0056	49.3±3.7	45.4±4.2	0.0305
Changes during						
Second visit	2.8±2.5	1.3±2.8	0.0227	5.6±1.6	2±2.4	0.0209
Third visit	6.5±2.6	1.6±5.1	0.0006	8.6±2.8	4.5±2.2	0.0465
% of changes during						
Second visit	7.5±7.8	2.9±5.9	0.0378	12.7±4.6	5.1±5.9	0.0033
Third visit	16.8±8.6	4.9±11.8	0.0015	20.9±8.8	11.0±13.2	0.047

It shows that Rosuvastatin 10mg is better than Atorvastatin 20mg in the reduction of LDL and also shows that Rosuvastatin 20mg is better than Atorvastatin 40mg in the reduction of LDL. Statistical analysis using student unpaired t-test shows that the p value is less than 0.05; the total cholesterol in patient between rosuvastatin and atorvastatin are found to be statistically significant. The comparison of LDL in rosuvastatin and atorvastatin patients was found to be statistically significant. (Table 3).

Table.3 Changes in LDL

LDL values at	Rosuvastatin 10mg	Atorvastatin 20mg	P value	Rosuvastatin 20mg	Atorvastatin 40mg	P value
First visit	117.7±18.1	127.8±22.2	0.2365	150.7±36.4	141.8±43.8	0.2538
Second visit	101.3±4.3	115.1±5.7	0.0392	128.9±2.3	122.7±1.9	0.0011
Third visit	95.3±2.7	110.4±5.9	0.0329	100.7±20.4	105.9±1.4	0.0082
Changes during						
Second visit	16.3±4.7	12.7±2.3	0.0355	21.8±2.5	19.1±1.9	0.039
Third visit	25.7±6.4	17.4±3.5	0.0027	50.9±4.7	36.5±6.5	0.0276
% of changes during						
Second visit	14.0±2.4	9.5±4.7	0.0404	14.6±4.2	10.5±3.1	0.0428
Third visit	22.6±3.3	16.6±4.1	0.0259	33±5.4	28±2.7	0.0277

It shows that Rosuvastatin 10mg is better than Atorvastatin 20mg in the reduction of Triglycerides and also shows that Rosuvastatin 20mg is better than Atorvastatin 40mg in the reduction of Triglycerides. Statistical analysis using student unpaired t- test shows that the p value is less than 0.05; the total cholesterol in patient between rosuvastatin and atorvastatin are found to be statistically significant. The comparison of LDL in rosuvastatin and atorvastatin patients was found to be statistically significant. (Table 4).

Table.4 Changes in TGL

TGL values at	Rosuvastatin 10mg	Atorvastatin 20mg	P value	Rosuvastatin 20mg	Atorvastatin 40mg	P value
First visit	192.7±38.1	191.9±32	0.8519	181.5±29.9	187.3±31.3	0.6935
Second visit	183.1±23.9	184.9±26.7	0.8357	165±21.6	176.9±23	0.8846
Third visit	172.1±6.2	187.1±7.4	0.0331	151.8±3.5	169.5±4.7	0.0438
Changes during						
Second visit	9.6±2.6	7.0±2.4	0.0485	16.5±6.3	11.3±7.2	0.0418
Third visit	20.3±4.0	4.8±5.7	0.0001	28.8±6.2	23.9±2.8	0.0277
% of changes during						
Second visit	2.5±13.4	1.5±21.6	0.3952	10.5±2.3	5.5±3.4	0.0319
Third visit	13.8±13.9	7.9±43.4	0.0318	20.8±4.0	10.1±6.3	0.0066

The comparison of Systolic BP in rosuvastatin and atorvastatin patients did not show any significant difference. (Table 5).

Table.5 Changes in Systolic BP

Systolic BP at	Rosuvastatin 10mg	Atorvastatin 20mg	P value	Rosuvastatin 20mg	Atorvastatin 40mg	P value
First visit	136.7±18.4	131.3±15.1	0.4341	133.3±17.2	143.3±13.5	0.1001
Second visit	133.3±9.8	130.7±11.6	0.5036	131.3±10.6	135.3±8.3	0.3352
Third visit	124.5±9.3	128±6.8	0.3664	131.7±5.8	131.5±6.9	1.0
Changes during						
Second visit	3.3±15.4	0.7±15.8	0.6362	2.0±15.2	8.0±9.4	0.099
Third visit	14.5±16.3	3.3±17.2	0.0968	3.3±16.7	13.1±11.1	0.1196
% of changes during						
Second visit	1.2±12.3	0.4±12.3	0.85	0.4±11.1	5.1±6.7	0.1494
Third visit	9.3±12.3	1.3±12.9	0.1503	1.1±12.1	8.6±7.1	0.1466

The comparison of Diastolic BP in rosuvastatin and atorvastatin patients did not show any significant difference. (Table 6).

Table.6 Changes in Diastolic BP

Diastolic BP at	Rosuvastatin 10mg	Atorvastatin 20mg	P value	Rosuvastatin 20mg	Atorvastatin 40mg	P value
First visit	76.7±8.2	76±9.1	0.7406	94.7±5.2	77.3±5.9	0.2184
Second visit	78±6.8	78.7±7.4	0.9052	76.7±4.9	78.0±4.1	0.4169
Third visit	76.4±5.0	78.9±5.2	0.2736	77.5±4.5	78.5±5.5	0.677
Changes during						
Second visit	1.3±11.3	2.7±16.6	0.6902	2.0±8.6	0.7±8	0.6269
Third visit	0.9±9.4	2.7±10.3	0.3541	2.5±8.7	1.5±8.0	0.6008
% of changes during						
Second visit	2.9±14.7	4.8±14.7	0.5787	3.3±11.6	1.5±10.6	0.6919
Third visit	0.1±13.7	4.9±14.4	0.319	4.0±11.7	2.5±11.0	0.6008

Relationship Between Lipid Profile And After Variables

Statistical analysis using student unpaired t- test shows that the p value is greater than 0.05; the drug used in diabetes mellitus and lipid profile patients were found to be statistically not significant. Statistical analysis using student unpaired t- test shows that the p value is greater than 0.05; the drug used in hypertension and lipid profile patients were found to be statistically not significant.(Table 7).

Table 7:Diabetes Mellitus, Hypertension and Lipid profile

DM	Total Cholesterol mg/dl		HDL mg/dl		LDL mg/dl		TGL mg/dl	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Present	216	15.3	39.0	5.5	131.3	27.7	194.7	67.6
Absent	212.2	18.4	41.6	3.9	136.1	36.4	185.2	64.2
P value	0.4512		0.0624		0.8691		0.5885	
Hypertensive Present	218.310.7		39.55.3		137.311.8		192.126.6	
Absent	214.910.1		41.93.9		13226		184.123.9	
P value	0.5631		0.6667		0.4999		0.662	

Relationship Between Blood Pressure And After Variables

The comparison of DM and BP in dyslipidemia patients did not show any significant difference. The comparison of Hypertension and systolic BP in dyslipidemia patients were found to be statistically significant. But the diastolic BP did not show any significant difference.(Table 8).

Table.8 Diabetes Mellitus, Hypertension and BP

DM	SBP mm Hg		DBP mm Hg	
	Mean	SD	Mean	SD
Present	141.0	15.5	78.5	5.9
Absent	133.8	16.4	75.0	7.5
P value	0.0836		0.0526	
Hypertensive Present	142.214.1		75.67.5	
Absent	129.316.3		75.76.9	
P value	0.002		0.6913	

DISCUSSION

In the present study, patients treated with rosuvastatin were more likely to attain lipid the lower level than were patients who received atorvastatin, which was statistically significant after accounting for baseline differences between groups. The rosuvastatin-treated patients continued to achieve significantly greater goal attainment rates before and after accounting for baseline differences. The results of the present study showed rosuvastatin to produce greater reductions in lipid levels, namely LDL cholesterol, Total cholesterol, HDL and Triglycerides goal attainment rates compared with atorvastatin. The present study found greater reduction in lipid level with Rosuvastatin 10-20mg compared with Atorvastatin 20-40mg. The study showed Rosuvastatin 10-20 mg to be a cost-effective alternative to Atorvastatin 20-40 mg, both in terms of cost per percentage lipid level reduction and cost per patient achieving. These results are in line with several previous cost-effectiveness analyses, which reported Rosuvastatin to be more cost effective than Atorvastatin, pravastatin and simvastatin. Further economic analyses of Rosuvastatin are now needed to determine its potential as a more cost-effective therapy compared with other statins. Rosuvastatin at doses of 10-20 mg was superior to atorvastatin 20-40 mg based therapies, as it reduced LDL-Cholesterol by more than the dose of atorvastatin .Similarly, it reduced triglycerides and total cholesterol more than atorvastatin therapy and increased HDL by the lower two doses more than was achieved on atorvastatin therapy. These results are better at lower but not at higher doses than these seen in the comparative study of statins in a general population, which showed equivalence of 10mg rosuvastatin and 20mg atorvastatin.

CONCLUSION

Patients treated with rosuvastatin had significantly greater reductions in LDL cholesterol, total cholesterol, triglycerides levels compared with those receiving atorvastatin. Patients receiving rosuvastatin were more likely to attain lipid goals compared with patients treated with atorvastatin. The recommended starting doses, rosuvastatin (10-20 mg) is more

efficacious than atorvastatin (20-40 mg), in terms of total cholesterol, HDL, LDL, and TG better in the lipid profile. The greater efficacy of rosuvastatin at starting dose should help to reduce the need for higher dosage and enable more Patients to achieve recommended treatment goals in clinical practice. Moreover there is, improvements in the whole lipid profile, including rise in HDLC.

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